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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/425,956	10/25/1999	RUDOLPH E. TANZI	0609.4110001	1225

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EXAMINER
DUFFY, PATRICIA ANN

ART UNIT	PAPER NUMBER
1645	20

DATE MAILED: 02/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/425,956	Applicant(s) Tanzi et al
	Examiner Patricia A. Duffy	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *11-20-02 and 1-16-03* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-30* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Continued Prosecution Application

1. The request filed on 11-20-02 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/425,956 is acceptable and a CPA has been established. An action on the CPA follows.

2. Claims 1-30 are pending and under examination.

3. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

4. Any rejection not reiterated herein is withdrawn based on Applicants' amendments.

Objections/Rejections Maintained

Drawings

5. This application has been filed with informal drawings which are acceptable for examination purposes only. The drawings are objected to by the draftsperson under 37 C.F.R. 1.84 or 1.152. See PTO-948 for details. Correction of the noted defects can be deferred until the application is allowed by the examiner.

Double Patenting

6. The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornum,* 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman,* 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) and © may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-16 and newly amended claims 17-30 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 5,972,634. Although the conflicting claims are not identical, they are not patentably distinct from each other because the term "antibody" of the patent is inclusive of both polyclonal and monoclonal antibodies.

Applicants indicate that a terminal disclaimer will be filed upon notice of a allowable subject matter. This is not persuasive, this rejection is not provisional and no allowable subject matter can be indicated until this rejection is overcome.

Claim Rejections - 35 U.S.C. § 112

8. Claims 5-16 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for all reasons made of record in Paper Nos. 11 and 15.

Applicants' arguments have been carefully considered but are not persuasive for reasons already made of record. Applicants argue that identifying the appropriate immunogens(s) and using them to generate the claimed antibodies (polyclonal antibodies that bind is specific to AB1-42 and does not cross react with Aβ1-40 or an antibody that is specific to Aβ1-40 that does not cross react with Aβ1-42) would have involved only routine experimentation in the art. Again this is not on point and not persuasive, Applicants specification must be enabled to make and use such an antibody, at the time the invention was made. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. Clearly from Applicants declaration and arguments, this specification was not enabled for how to make the antibodies for use in the method, since the immunogen for the production of polyclonal antibodies is not set forth at the time it was filed. For, the production of antibodies, the particular immunogen used to produce such requires specific written description in order to enable how to make the antibody. This specification, as originally filed, fails to teach how to make the claimed antibodies because if lacks an adequate written description of the immunogen to produce such. It is noted that these unique immunogens are not described by this specification. Reliance on the skill of the art to determine the immunogen and test for operability is not persuasive to remove this rejection because; as also recognized by the Federal Circuit:

> "However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material *or of any conditions under which a process can be carried out,* [emphasis added] undue experimentation is required; there is a failure to meet the

> enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research."(Genentech Inc. v. Novo Nordisk A/S Ltd., 42 USPQ2d 1001).

Further, the courts have held in Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.) because the specification has no written description of the immunogen to produce the polyclonal antibodies of the invention and Declarant admits that one would have to perform further experimentation to discover such. Because of the lack of written description of the starting material (the immunogen to produce the polyclonal antibodies with the claimed binding specificity), the specification is not enabled for how to make. This issue can not be resolved by applicants alleging that the identification of such is within the skill in the art. Applicant argues and reminds the examiner that the specification need not supply information that is well known in the art. While this is true, the examiner points out that the immunogen to produce the polyclonal antibodies with the specific binding pattern are not know in the art. As such, in contrast to applicants assertions, the immunogen is not common and well known as if it were written out in the patent and delineated in the drawings. If this were so, Declarant would not have attested that one would have to discover the appropriate immunogen to produce the polyclonal antibodies with the claimed binding specificity. Applicants argue that the skilled artisan would know where to search

for any needed starting materials. This is not persuasive, the needed starting materials (i.e the immunogen) is not set forth in the specification and as such one skilled in the art would not know where to search for such. Applicants argue that since one of skill in the at could have easily obtained the immunogens needed to generate polyclonal antibodies, the specification is enabled. This is not persuasive for all the reasons previously set forth. The lack of written description of such an immunogen to produce the antibodies is not set forth in the specification and is acknowledged not to have been by Declarant. Therefore, the claims specifically recite subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants also assert that a prima facie case for non-enablement has not been provided because no evidence or scientific reasoning has been provided. This is not persuasive, Applicants are directed to the evidence and scientific reasoning set forth in Paper Nos 11 and 13 and the responses set forth therein. Applicants are reminded that polyclonal antibodies are a collection of antibodies with different binding specificities and as such are fundamentally different for monoclonal antibodies. The skilled artisan is well aware of the exquisite specificity of monoclonal antibodies as compared to polyclonal antibodies. It is the particular screening process that identifies monoclonal antibodies with the appropriate binding specificity, screening for others is routine. In contrast, the same immunogen would not produce a polyclonal antibody with the claimed binding specificity, because the immunogen would produce a polyclonal antibody that is a collection of antibodies with overlapping specificities. These overlapping specificities can not be "screened out", they are either present or absent. Applicants screening tool for monoclonal antibodies, does not work for polyclonal antibodies since the sub-specifities can not be removed by merely

testing binding as was set forth in this specification for monoclonal antibodies. It is further noted that the immunogens described at page 5, lines 7-19 to make antibodies that bind the 1-42 but not the 1-40 species is not persuasive, because it is well known in the art that the smallest synthetic peptide that will consistently elicit antibodies that bind to the original protein are 6 residues in length (see Harlow et al, Antibodies A Laboratory Manual, Cold Spring Harbor Press, Inc.). Using larger peptides, necessarily encompasses residues in the 1-40 regions and as previously set forth, this immunogen used would produce a polyclonal antibody with a wide range of specificities that include both species. Given the fundamental overlap of the specificities, the polyclonal antibody produced by the immunogens disclosed, can not and would not have the claimed binding specificity. Further, there is no immunogen that would allow for the production of a 1-40 specificity that does not bind the 1-42, since the residues in 1-40 are necessarily encompassed in the 1-42 species. The examiner has appropriately cited evidence and sound scientific reasoning which is reason to doubt the objective truth of the statements contained in applicants specification. (*In re Marzocchi and Horton*, 169 USPQ 367 (CCPA 1971)). A *prima facie* case of non-enablement has been set forth. The examiner maintains in the absence of an adequate written description of the immunogen to produce the claimed polyclonal antibodies with the claimed binding specificity, the specification is fundamentally non-enabled.

The rejection is maintained.

9. Claims 5-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification lacks adequate written description of the necessary immunogens and process steps to produce the polyclonal antibody (polyclonal antibodies that bind is specific to AB1-42 and does not cross react with Aβ1-40 or an antibody that is specific to Aβ1-40 that does not cross react with Aβ1-42) with the claimed specificities for use in the assay. The specification as originally filed lacks a written description of how to make such. The specification lacks any description of the polyclonal antibodies that are used in the methods of the invention. These polyclonal antibodies are required to perform the method. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In this case, the lack of adequate written description of the immunogen used to make the claimed polyclonal antibodies indicates to one of skill in the antibody art that at the time the application was filed, Applicants did not have possession of the claimed antibodies for use in the method of the invention.

Status of Claims

10. All claims stand rejected.

Conclusion

11. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should

applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Thursday and Saturday from 10:30 AM to 7:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached at (703) 308-3909.

Patricia A. Duffy, Ph.D.
February 4, 2003

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600